

Oct 14 2003 9:33AM CLAIMS RELATIONSHIP

10.1070-001

PG3692USW  
S/N 10/018,700

In the claims:

Please amend the claims as follows:

1-14 (Cancelled)

15. (currently amended) A method for the propagation of lytic organisms, comprising:

- a) providing a hollow fiber bioreactor containing multiple hollow fibers, and having a stable cell line growing in the extracapillary space (ECS) of said hollow fiber bioreactor at a cell density of 10<sup>6</sup> cells per milliliter or greater;
- b) introducing a lytic organism into said ECS, said lytic organism of a type capable of infecting said stable cell line; and
- c) allowing said lytic organism to infect, and multiply within, the cells of the stable cell line.

16. (canceled)

2 16. (previously presented) A method according to claim 15 where said stable cell line is selected from mammalian cell lines, insect cell lines, yeast cell lines and bacterial cell lines.

3 16. (previously presented) A method according to claim 16, further comprising harvesting said lytic organism from the hollow fiber bioreactor.

7 19. (currently amended) A method according to claim 15 for the propagation of lytic organisms, comprising:

100-14-0001-0010AM CLAIM 15/16/17

DO. 1361

PG3692USW  
S/N 10/018,700

(a) providing a hollow fiber bioreactor containing multiple hollow fibers, and having a stable cell line growing in the extracapillary space (ECS) of said hollow fiber bioreactor;

(b) introducing a lytic organism into said ECS, said lytic organism of a type capable of infecting said stable cell line, and where wherein said lytic organism contains nucleic acid encoding a protein of interest that is expressed in the stable cell line following infection by the lytic organism;

(c) allowing said lytic organism to infect, and multiply within, the cells of the stable cell line.

8 26. (previously presented) A method according to claim 19 further comprising the step of harvesting said protein of interest from the hollow fiber bioreactor.

16 21. (currently amended) A method according to claim 15 for the propagation of lytic organisms, comprising:  
(a) providing a hollow fiber bioreactor containing multiple hollow fibers, and having a stable cell line growing in the extracapillary space (ECS) of said hollow fiber bioreactor;

(b) introducing a lytic organism into said ECS, said lytic organism of a type capable of infecting said stable cell line, and where;

(c) allowing said lytic organism to infect, and multiply within, the cells of the stable cell line, and where stable cell line survives in the hollow fiber bioreactor for at least 10 days after infection.

17 22. (currently amended) A method according to claim 15 claim 21 where said stable cell line survives in the hollow fiber bioreactor for at least 15 days after infection.

CON. 14 2000 8:11 AM CLAUDIO NELLO DUE

66-1970-1

PG3692USW  
S/N 10/018,700

*18*  
*23.* (currently amended) A method according to claim 15 claim 21 where said stable cell line survives in the hollow fiber bioreactor for at least 20 days after infection.

*6*  
*24.* (previously presented) A method according to claim *18* further comprising, after said harvest, repopulating said hollow fiber bioreactor with said stable cell line remaining after the harvest.

25. (canceled)

*4*  
*26.* (previously presented) A method according to claim *15* where said lytic organism is a virus.

*25*  
*27.* (previously presented) A method according to claim *26* where said virus is a baculovirus.

*26*  
*28.* (previously presented) A method according to claim *26* where said virus is an adenovirus.

29. (canceled)

*27*  
*30.* (previously presented) A hollow fiber bioreactor comprising: multiple hollow fibers arranged to form an extracapillary space (ECS); a stable cell line growing in said ECS at a density of at least  $10^6$  cells per milliliter; and a lytic organism of a type capable of infecting and lysing cells of said stable cell line.

31. (canceled)

JUL 14 2003 9:21AM CLAUDIO WELLCOME

WIL 1953 3 1

PG3692USW  
S/N 10/018,700

9 7  
32. (new) A method according to claim 19 where said stable cell line has established a cell density within the ECS of  $10^6$  cells per milliliter or greater prior to introduction of the lytic organism.

24 16  
33. (new) A method according to claim 21 where said stable cell line has established a cell density within the ECS of  $10^6$  cells per milliliter or greater prior to introduction of the lytic organism.

10 7  
34. (new) A method according to claim 19 where said stable cell line is selected from mammalian cell lines, insect cell lines, yeast cell lines and bacterial cell lines.

19 16  
35. (new) A method according to claim 21 where said stable cell line is selected from mammalian cell lines, insect cell lines, yeast cell lines and bacterial cell lines.

11 7  
36. (new) A method according to claim 16, further comprising harvesting said lytic organism from the hollow fiber bioreactor.

20 16  
37. (new) A method according to claim 21, further comprising harvesting said lytic organism from the hollow fiber bioreactor.

5 1  
38. (new) A method according to claim 15 where said stable cell line survives in the hollow fiber bioreactor for at least 10 days after infection.

12 7  
39. (new) A method according to claim 19 where said stable cell line survives in the hollow fiber bioreactor for at least 10 days after infection.

JUL 14 2003 11:14 AM PLANO WELLCOME

PLANO

PG3692USW  
S/N 10/018,700

- 13 7  
40. (new) A method according to claim 19 where said lytic organism is a virus.
- 14 7  
41. (new) A method according to claim 19 where said lytic organism is a baculovirus.
- 15 7  
42. (new) A method according to claim 19 where said lytic organism is an adenovirus.
- 21 16  
43. (new) A method according to claim 21 where said lytic organism is a virus.
- 22 16  
44. (new) A method according to claim 21 where said lytic organism is a baculovirus.
- 23 16  
45. (new) A method according to claim 21 where said lytic organism is an adenovirus.
- 28 27  
46. (new) A hollow fiber bioreactor according to claim 30, where said stable cell line is selected from mammalian cell lines, insect cell lines, yeast cell lines and bacterial cell lines.
- 29 27  
47. (new) A hollow fiber bioreactor according to claim 30 where said lytic organism is a virus.
- 30 27  
48. (new) A hollow fiber bioreactor according to claim 30 where said lytic organism is a baculovirus.

10/14/03 8:41AM PLANO WELLCOME

PLANO TX

PG3692USW  
S/N 10/018,700

31<sup>46</sup> (new) A hollow fiber bioreactor according to claim 30 where said  
lytic organism is an adenovirus.

27